APPENDIX C: NUMBERS OF SUBMISSIONS

This section describes the method that is used to approximate the number of reporting submissions that would be required under the rule. Estimates of the number of microorganisms reportable to EPA are primarily based on the ICF Survey of Biotechnology Companies (ICF 1988--see Appendix A). The ICF survey developed information based on the categories of microorganisms established in the 1986 Policy Statement, under which the use of intergeneric microorganisms triggers reporting. Under the rule, intergeneric microorganisms also would be subject to reporting.

There is some uncertainty associated with predicting the numbers of microorganisms that would be subject to reporting because of the fledgling nature of the TSCA biotechnology industry. Future growth of this segment of the biotechnology industry depends on unpredictable factors such as the rate of scientific breakthroughs, the evolution of public attitudes toward genetically engineered microorganisms, progress in scientific knowledge about risks, and trends in state regulation. To some extent, industry growth may also depend on the outcome of this rulemaking. Some of the sources of this uncertainty are addressed in the sensitivity analysis (see Appendix D).

Some types of microorganisms identified in the survey are not included in the estimated numbers of submissions. The assumptions used to decide which microorganisms are included are as follows:

- It is assumed that contained microorganisms associated with reagent production do not require submissions. Most of these microorganisms would be exempt because products are sold for research purposes, only. Some reagents are likely to be sold for uses other than R&D, however, such that excluding all of these microorganism products could understate submission numbers;*

* Microorganisms associated with reagent production are included in the calculation of the TSCA industry growth rate. They are excluded from the calculation of the other growth rates.

- Except for microorganisms associated with reagent applications, all intergeneric microorganisms intended for general commercial use are assumed to require submissions;
- The number of submissions that would be considered "released" as a result of failure to meet general rule containment definitions (e.g., for pilot scale fermentation) was assumed to be zero;
- Submissions resulting from related strains were not quantified.*

A. Estimating the Growth Rates

Several growth rates are used to project future activity in the segment of the biotechnology market covered by TSCA. Each of these growth rates is calculated independently because the various sectors of the TSCA biotechnology market have significantly different expectations for progress. The data used to calculate these growth rates are taken primarily from the 1988 ICF survey (ICF 1988). The 1988 ICF survey focused on designations of intergeneric versus intrageneric microorganisms as identified in the 1986 policy statement and is used as the basis for predicting growth in the numbers of projects and submissions expected over time under the rule.

As discussed in the introduction to this appendix, present calculations of submission growth rates are based upon derivations from the categories of microorganisms presented in the ICF survey. Data used to calculate growth rates also are based on information recently obtained in 1991 from industry sources. Specifically, in the ICF survey, respondents gave the number of products currently in R&D and expected to be in R&D in 5 years. In 1991, industry sources were contacted again and asked about their progress in TSCA market areas and their current R&D activity. This revised information was used to adjust the 1988 survey estimates for product R&D in 5 years. In most

* "Related strains" are similar strains that are part of a single research program leading to a commercial released microbial product. The survey did not distinguish "first-time" strains from "related" strains. This analysis assumes that each product reported in the survey potentially could lead to a separate commercial product.

cases, no adjustments were necessary because the new information is consistent with the trends implied by the 1988 survey data. In two TSCA market areas, however, the agricultural market and the biomass conversion market, modifications are made to the Year 5 stock of microorganisms according to this current information.

For the TSCA agricultural market as a whole, the 1988 survey implied a decline of about 4.5 percent per year but products using intergeneric and intrageneric manipulations were expected to increase by about 4.5 percent per year. These trends, based on 1988 data, imply a shift toward recombinant manipulations involving more sophisticated biotechnology techniques that the data based on the 1991 survey do not support (IBA 1991, Biotechnica 1991, Urbana 1991, Surax 1991).

A similar adjustment is made in the expectations in the biomass conversion market. The overall market decline derived from the survey was expected to be about 19 percent per year, but recombinant products were only expected to decline at 2.5 percent per year. Again, the 1991 information indicates that the trend towards recombinant products has not been fulfilled (IBA 1991, Envirogen 1991b, Alpha-Beta 1991).

For both these market areas, the analysis makes the conservative assumption that the overall decline in the market is not greater than implied by the 1988 survey, and the products in those areas predicted to be in R&D in 5 years are reallocated to follow the same distribution as the base stock of products in the survey.

Growth rates for the sectors are then derived from the data as follows:

- the growth rate for "new" environmental applications of TSCA microorganisms is derived from the stock of intergeneric microorganisms involved in released projects;
- the growth rate for "new" fermentation-system applications of TSCA microorganisms is derived from the projected activities involving

intergeneric contained products; and

- the industry growth rate for the TSCA biotechnology industry is derived from all products in the markets covered by TSCA, including naturally occurring microorganisms and biotech reagents.

The appropriate rates are then determined using the following formula:

$$rate = \sqrt[5]{\frac{stock_{expected}}{stock_{reported}}} - 1$$

The growth rate derived from the above analysis and area of use for each rate in the RIA are as follows:

- environmental applications of "new" TSCA microorganisms (1 percent), used to project the numbers of TERAs as well as MCANs resulting from these projects;

- fermentation-system applications of " new" TSCA microorganisms (10 percent), used to estimate the numbers of MCANs resulting from these fermentation-system activities;

- the TSCA segment of the biotechnology industry as a whole (4 percent), used to project the numbers of new companies that will require rule familiarization and special documentation costs.

Table C-1 presents the sector specific rates that are calculated with their definitions under the rule, and the areas of the RIA to which they apply. Note that as the degree of oversight changes in the other options, the rate for a particular sector may be affected.

B. Projecting TERA Submissions

In order to estimate Year 1 and Year 5 stocks of R&D microorganisms for the rule, the 1 percent growth rate for "new" environmental applications is applied to the estimated number of "new" environmental application products in R&D from the 1988 survey (11). Using the assumption that these products take an average of 5 years to develop, Year 1 stocks (12) and Year 5 stocks (13) are converted to a flow by dividing by 5, resulting in 3 first-time industry TERAs for both Year 1 and Year 5. Information obtained in 1991 also suggests

Table C-1. Growth Rates for the Final Rule

Industry sector	annual change	Derivation	RIA area of use
New Environmental applications	1%	All intergeneric released products[a]	TERAs, commercial submissions
New Fermentation-system applications	10%	All intergeneric contained products[a]	Commercial submissions
TSCA Industry	4%	All sectors, including projects using naturally occuring microorganisms and biotechnology reagents	Rule familiarization, special documentation

[a] Does not include microorganisms associated with reagent production

Sources: Appendix A and Appendix B.

that an average project would require 3 follow-on TERAs. For accounting purposes, all follow-ons are assumed to occur in the same year as the first submission so that there are 9 industry follow-ons in both Year 1 and Year 5. It is assumed that university R&D work mirrors industry work and thus the number of TERAs is multiplied by 2*. The projected numbers of R&D submissions are shown in Table C-2.

Although R&D releases of microorganisms can be reported as either TERAs or MCANs, this analysis assumes that all R&D submissions will be TERAs, for the following reasons:

- TERAs have a target review period of 60 days (extendable by EPA for "good cause"). The MCAN review period is mandated at 90 days in the Toxic Substances Control Act and can be extended by EPA for another 90 days.**
- If a TERA is reviewed in less than 60 days, the microbial release can proceed as soon as EPA gives approval. For MCANs, even if the review is completed in fewer than 90 days, manufacture cannot begin before the 90-day period has expired.
- There are no TERA user fees. MCAN user fees are $2,500 for a single MCAN or consolidated group of MCANs. User fees for MCANs are $100 for small businesses with annual sales of $40 million or less (see Chapter VIII).
- The TERA is expected to allow greater flexibility in varying the genetic construct without triggering a new submission. This is because the range of permitted variations depends on the TERA and TERA Agreement, and can be broad when the Agency has low risk concerns.
- TERA Agreements should require less time to negotiate than a Consent Order because submissions for R&D projects most likely will have lower exposure profiles than those for commercial projects.

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* Under the rule, the Agency defines "commercial purposes" by a set of commercial indicia, described in Chapter IV.

** Although the TERA review period may appear more open-ended than the MCAN review period, in practice, PMN review periods have sometimes lasted more than 180 days when a company has voluntarily agreed to "stop the clock".

Table C-2. Submissions for R&D Microorganisms

	1988 Survey	Year 1	Year 5
R&D Stock of New environmental applications	11	12	13
Industry			
First-time TERAs		3	3
Follow-on TERAs		9	9
University			
First-time TERAs		3	3
Follow-on TERAs		9	9
Total			
First-time TERAs		6	6
Follow-on TERAs		18	18

Sources: Appendix A and Appendix B.

- Modifications to the TERA Agreement are expected to be faster than modifications to the Section 5(e) Consent Order that would be required for MCAN submissions.

C. Projecting the Number of Commercial Submissions

Some portion of the stock of microorganisms projected to be in R&D use will "graduate" to commercial use, and therefore will be subject to commercial reporting. The industry stocks of products in R&D are calculated for Year 1 and Year 5, and converted into a flow in the same manner as for R&D submissions, with the additional assumption that the transition to commercial products is based on a 50 percent failure rate.

In addition to the environmental applications subject to R&D reporting that ultimately reach commercialization, commercial submissions include those for fermentation-system applications. The growth rate for these applications is higher (10 percent) than for the environmental applications. In addition, fermentation-system products are only expected to average 2 years in R&D. The number of "new" fermentation-system applications is then calculated in the same manner described above.

The projected numbers of submissions at the general commercial use level for both "new" environmental and "new" fermentation-system applications are shown in Table C-3. As the table indicates, commercial submissions under the rule are distributed among MCANs and Tier I and II exemptions according to the following percentages: 20 percent MCANs; 40 percent Tier I exemptions; and 40 percent Tier II exemptions (EPA, 1991).

D. Submission Projections for Regulatory Alternatives

The projections for the numbers of submissions under the regulatory alternatives were made using the same procedure. Because the extent of oversight varies between these alternatives, the sectors of the TSCA market that are subject to reporting requirements and the growth rate and other

Table C-3. Commercial Submissions

	1988 Survey	Year 1	Year 5
R&D Stock of New environmental applications	11	12	13
R&D Stock of New fermentation-system applications	43	77	112
Commercial Product Submissions		22	30
MCANs		4	6
Tier I exemptions		9	12
Tier II exemptions		9	12

Sources: Appendix A and Appendix B.

assumptions for these sectors varies between the different options. As a result, the distribution of commercial submissions for several of these options may differ from that of the rule. This analysis, however, assumes that these regulatory alternatives will result in the same distribution of MCANs, Tier I Exemptions, and Tier II Exemptions as the rule. Table C-4 presents the growth rates and other assumptions that are used to make the submission projections for each option. Table C-5 presents the numbers of submissions expected for each option.

E. Projecting Final Rule Familiarization and Recordkeeping

The size of the regulated community is based on the 72 companies identified by the 1988 ICF Survey plus the 306 universities receiving NIH funding for rDNA biotechnology research. All companies and universities are assumed to be subject to rule familiarization costs. These numbers and the growth rate of 4 percent for the portion of the industry subject to TSCA are used to estimate the size of the regulated community subject to rule familiarization in Year 1 and Year 5. The analysis assumes that the number of universities does not change over time. (Because data were not available to determine how many of the 306 universities identified would actually be involved in TSCA related research for commercial purposes, it is likely that rule familiarization costs attributed to such institutions are overstated).

Table C-4. Assumptions Used to Project Submissions for Regulatory Alternatives

Assumption[a]	Preferred	Current	Alt. 1	Alt. 2	Alt. 3
Growth Rates					
Industry	4%	4%	4%	4%	4%
New Environmental Applications	1%	1%	1%	-1%	-1%
New Fermentation-system Applications	10%	10%	10%	4%	4%
Years of R&D for New Environmental Applications	5	5	5	2	2
Years of R&D for New Fermentation-system Applications	2	2	2	1	1
Follow-ons per TERA	3		3	1	1
R&D to Commercial Dropout rate	50%	50%	50%	30%	30%
Commercial Submission Distribution[b]	20%	100%	100%	20%	100%
MCAN	40%			40%	
Tier I	40%			40%	
Tier II					
Percentage of R&D Field Tests requiring monitoring	100%		100%	100%	100%

[a] The changes in these assumptions between alternatives reflect the different expectations for the sectors of the biotechnology market that would be subject to various requirements as the breadth of the rule changes.

[b] The distribution of commercial submissions (i.e., 20 percent MCANs, 20 percent Tier Is, and 40 percent Tier IIs) that was estimated for the final rule has been carried through to Alternative 2 because no data were available to help predict the distribution of submissions for this alternative.

Table C-5. Projected Submissions for Regulatory Options

	Current Regulatory Environment [a]	Alternative 1	Alternative 2	Alternative 3
Year 1				
First-time TERAs		6	74	74
Follow-on TERAs		18	74	74
MCANs	22	22	37	185
Tier I exemptions			74	
Tier II exemptions			74	
Year 5				
First-time TERAs		6	72	72
Follow-on TERAs		18	72	72
MCANs	30	30	42	212
Tier I exemptions			85	
Tier II exemptions			85	

[a] Submissions would be PMNs in the current regulatory environment.